



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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| (51) International Patent Classification ⁶ : A61K 39/12, 38/16, 39/245, 39/385 | A3 | (11) International Publication Number: WO 99/58145 (43) International Publication Date: 18 November 1999 (18.11.99) |
| (21) International Application Number: PCT/GB99/01461 (22) International Filing Date: 10 May 1999 (10.05.99) (30) Priority Data: 9809958.3 8 May 1998 (08.05.98) GB 9811954.8 3 June 1998 (03.06.98) GB 9812316.9 8 June 1998 (08.06.98) GB (71) Applicant (for all designated States except US): UNIVERSITY OF BRISTOL [GB/GB]; Senate House, Tyndall Avenue, Clifton, Bristol BS8 1TH (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): HIRST, Timothy, Raymond [GB/GB]; 30 Albert Road, Clevedon, North Somerset BS21 7RR (GB). WILLIAMS, Neil, Andrew [GB/GB]; 16 Old Coach Road, Cross, Axbridge, Somerset BS26 2EF (GB). (74) Agent: NASH, David, Allan; Haseltine Lake & Co., Imperial House, 15-19 Kingsway, London WC2B 6UD (GB). | | (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 3 February 2000 (03.02.00) |
| (54) Title: IMMUNOMODULATORS FOR VACCINES (57) Abstract <p>There is disclosed the use of: (i) EtxB, CtxB or VtxB free from whole toxin; (ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or (iii) an agent having an effect on intracellular signalling events mediated by GM1-binding or Gb3 binding; as an immunomodulator for a vaccine against infectious diseases.</p> | | |

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INTERNATIONAL SEARCH REPORT

International Application No.
PCT/GB 99/01461

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K39/12 A61K38/16 A61K39/245 A61K39/385

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| Y | WO 97 02045 A (UNIVERSITY OF BRISTOL) 23 January 1997 (1997-01-23) cited in the application page 44 -page 46 --- | 1-36 |
| Y | NASHAR T O ET AL: "Modulation of B-cell activation by the B subunit of Escherichia coli enterotoxin: receptor interaction up-regulates MHC class II, B7, CD40, CD25 and ICAM-1." IMMUNOLOGY, (1997 AUG) 91 (4) 572-8. , XP002123821 the whole document --- -/-- | 1-36 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

25 November 1999

Date of issuing of the international search report

15/12/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Moreau, J

INTERNATIONAL SEARCH REPORT

Int: onal Application No

PCT/GB 99/01461

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| X | <p>HIRST T R ET AL: "Cholera toxin and related enterotoxins as potent immune modulators." SOCIETY FOR APPLIED BACTERIOLOGY SYMPOSIUM SERIES, (1998) 27 26S-34S, XP000856429 the whole document</p> <p>---</p> | 1-36 |
| X | <p>EP 0 372 928 A (UNIVERSITY OF LEICESTER) 13 June 1990 (1990-06-13) claims 1-14</p> <p>---</p> | 1,24, 28-30 |
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| X | <p>ZHANG T ET AL: "ORAL IMMUNIZATION WITH THE DODECAPEPTIDE REPEAT OF THE SERINE-RICH ENTAMOEBA HISTOLYTICA PROTEIN (SREHP) FUSED TO THE CHOLERA TOXIN B SUBUNIT INDUCES A MUCOSAL AND SYSTEMIC ANTI-SREHP ANTIBODY RESPONSE" INFECTION AND IMMUNITY,US,AMERICAN SOCIETY FOR MICROBIOLOGY. WASHINGTON, vol. 63, no. 4, page 1349-1355 XP000645273 ISSN: 0019-9567 the whole document</p> <p>---</p> | 1,22,24, 26,28-30 |
| P,X | <p>WILLIAMS N A ET AL: "Immune modulation by the cholera-like enterotoxins: from adjuvant to therapeutic." IMMUNOLOGY TODAY, (1999 FEB) 20 (2) 95-101, XP002123822 the whole document</p> <p>---</p> | 1-36 |
| P,X | <p>NASHAR T O ET AL: "Importance of receptor binding in the immunogenicity, adjuvanticity and therapeutic properties of cholera toxin and Escherichia coli heat-labile enterotoxin." MEDICAL MICROBIOLOGY AND IMMUNOLOGY, (1998 JUN) 187 (1) 3-10, XP000857029 the whole document</p> <p>---</p> | 1-36 |
| P,X | <p>RICHARDS C M ET AL: "Induction of mucosal immunity against herpes simplex virus type 1 in the mouse protects against ocular infection and establishment of latency." JOURNAL OF INFECTIOUS DISEASES, (1998 JUN) 177 (6) 1451-7. , XP002123823 cited in the application the whole document</p> <p>---</p> | 1-36 |
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 99/01461

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
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| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| E | EP 0 919 243 A (DUPHAR INTERNATIONAL RESEARCH) 2 June 1999 (1999-06-02) the whole document --- | 1-36 |
| E | WO 99 36088 A (MAXIM PHARMACEUTICALS) 22 July 1999 (1999-07-22) the whole document ----- | 1-36 |

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 99/01461

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 1-23,30,31,34 and 35 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/01461

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
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